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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/679,776	10/05/2000	Richard D. Granstein	2650/1F966-US1	8709

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EXAMINER	
LI, QIAN JANICE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 03/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/679,776	GRANSTEIN, RICHARD D.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 October 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Declaration of Richard D. Granstein, amendment, and response submitted on December 15, 2003 has been entered. Claims 2-7, 11, 12, 16-19, 21-23, and 31 have been cancelled; claims 32-49 are newly submitted, pending, and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims, arguments and the Declaration will not be reiterated. The arguments would be addressed to the extent that they apply to current rejection.

Claim Objections

Claims 44 and 45 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 43 recites "antigen RNA", claims 44 and 45 depend from claim 43, and recites total "cellular" RNA/mRNA, which are broader in scope compared to the "antigen" RNA. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Certain aspect of the prior rejection of claims 1-31 in Paper #17 is reinstated and now applies to claims 32-36 under 35 U.S.C. 112, first paragraph because the specification, while being enabling for inducing an immune response to a tumor in a subject by *intradermal* or *subcutaneous* administration of total tumor cell RNA, wherein the tumor cells are autologous or taken from the same type of allogenic tumors, does not reasonably provide enablement for doing so by any route of administration to epidermal cells of the subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims, for reasons of record and following.

In the response to the rejection of Paper #17, applicants indicated that the claims as written indicate that the claims exclude other routes of administration.

Upon further consideration, this argument is found not persuasive since, in patentability context, claims are to be given their broadest reasonable interpretations, and since limitations are not to be read into claims from specification. Case law has stated that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Accordingly, the rejection is reinstated and applies to new claims 32-36.

Claims 43-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inducing tolerance to an allogenic transplant

antigen in a subject by intravenously administering total cellular RNA or total cellular mRNA at least seven days prior to the allogenic transplantation, wherein the cells are from the graft tissue or spleen, does not reasonably provide enablement for inducing tolerance to a xenogenic transplant antigen, an autoantigen, and an allergen by intravenous administering antigen RNA or total RNA/mRNA from any somatic cells at any time. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are drawn to inducing tolerance to an antigen in a subject, wherein the antigen is an autoantigen, an allergen or a transplant tissue antigen. Given the broadest reasonable interpretation that is consistent with the specification, claims are drawn to therapeutic methods for treating autoimmune diseases, allergy, and preventing graft rejection from both allogenic and xenogenic sources. However, the specification and the Declaration fail to provide support for the full scope of the claims. This is because as indicated in the first Office action and reiterated here, tolerance induction involves complicated immune regulation. It is well known that the human immune system has a sophisticated mechanism of self and non-self recognition and self-tolerance, a complex negative selection and autoreactive cell-elimination process. Induction of tolerance requires many factors working in concert, such as the type of antigen, the amount of antigen, the timing of antigen priming, and the state of host immune system etc. It would have required extensive undue experimentation for one

skilled in the art to use the claimed invention to induce tolerance to any antigen, in any subject.

The Remarks filed 12/15/03 relies on the Declaration and example 4 of the specification, which will be addressed as following.

With regard to inducing tolerance to transplant antigen, the specification and the Declaration fail to support the full scope of the claims because the claims encompass preventing xenogenic rejection, and it is known in the art that xenogenic rejection response is fast, intense and vigorous, although the Declaration illustrated reduced allogenic skin graft rejection (points 6 & 7), the rejection response has not been ablated. With regard to incorporate allogenic and xenogenic cells in the instant implants, there are still major barriers for successful transplantation as of post-filing dates. *Game et al* (Wien Klin Wochenschr 2001;113:823-38) detailed different types of allogenic and xenogenic rejection (hyperacute, acute, chronic) and underlying mechanisms involving multiple pathways that lead to the failure of allogenic and xenogenic transplantation, and states, "WHILE MAJOR IMPROVEMENTS HAVE BEEN MADE IN THE PREVENTION AND TREATMENT OF HYPERACUTE AND ACUTE TRANSPLANT REJECTION, MOST GRAFTS WILL SUCCUMB TO CHRONIC REJECTION: THIS REFLECTS THE EXTENT OF OUR KNOWLEDGE OF THE MECHANISMS THAT DRIVE THESE PROCESSES", as for xenotransplantation, "NOVEL APPROACHES HAVE OVERCOME SOME EARLY ANTIBODY MEDIATED REJECTION EVENTS BUT THEN REVEAL A HUGE, INTENSE, ADAPTIVE CELLULAR RESPONSE". *Platt et al* (Nat Biotech 2002 Mar;20(3)231-2) clearly teach, "UNFORTUNATELY, SOLVING THE PROBLEM OF HYPERACUTE REJECTION DOES NOT MAKE XENOTRANSPLANTATION FEASIBLE, BUT RATHER REVEALS A MORE VEXING PROBLEM CALLED ACUTE VASCULAR REJECTION. ACUTE VASCULAR REJECTION, LIKE HYPERACUTE REJECTION, IS TRIGGERED

BY ANTI-DONOR ANTIBODIES; HOWEVER, IN CONTRAST TO HYPERACUTE REJECTION, THESE ANTIBODIES ARE NOT DIRECTED EXCLUSIVELY AGAINST α1,3GAL, AND THE INVOLVEMENT OF THE COMPLEMENT SYSTEM IS FAR MORE SUBTLE" The specification fails to teach whether the claimed method would overcome the aforementioned difficulties in the art, in light of the nature of the xenotransplant rejection and the state of the prior and post-filing art, it is highly unpredictable whether administering the total cellular RNA/mRNA could reduce the xenotransplant rejection to the extend that a therapeutic effect could be obtained. It would have required undue experimentation for the skilled artisan intending to practice the instant invention.

Claims are drawn to using cellular RNA from any somatic cells, and the Declaration only show that the cellular RNA from spleen cells could reduce the allogenic rejection, this appears to be significant because specificity is a hallmark of acquired immunity/tolerance, and the spleen cells contain mostly cells of immune system, which actively participate in a graft rejection response. The specification or Declaration fail to teach whether total cellular RNA from *any* somatic cell type such as muscle cells would also prevent a skin graft rejection. Moreover, the timing of the RNA administration appear to be critical because it is a well known in the art that it takes at least 7 to 14 days to trigger an effective immune response, it is unpredictable whether the administration right before, at the same time, or after the transplantation would also reduce an allogenic rejection. In view of such, the specification and the Declaration fail to support the full scope of the claims.

With respect to inducing tolerance to autoantigen and allergen, unlike the graft recipient, who ordinarily would have a normal immune system, patients suffering from allergy and autoimmune disease have an abnormal immune system, the occurrence of an autoimmune disease symbols a breakdown of the sophisticated mechanism of self and non-self recognition and self-tolerance and a breakdown of the complex negative selection and autoreactive cell-elimination process in a subject. Comparable to the autoimmune disease is the allergy, i.e. a hypersensitive response of the immune system to an antigen, many factors including genetic, environmental, and others such as route of contact contribute to the onset of allergy. *Kalden et al* (Advances in Immunology, 1998;68:333-395, paragraph 2 through page 396 paragraph 4). "EVEN RELATIVELY "SIMPLE" EXPERIMENTAL MODELS OF AUTOIMMUNITY REMAIN DIFFICULT TO TREAT", AND "THE EXPERIMENTAL MODELS OF AUTOIMMUNE DISEASES ARE CLEARLY DISTINCT DISORDERS OF HIGHLY STRUCTURED AUTOIMMUNITY; DESPITE THE FACT THAT THEY SHARE SOME IMMUNOPATHOGENETIC PATHWAYS, THEY RELY ON QUITE DIFFERENT POLYGENETIC BACKGROUNDS. THUS, THE BENEFICIAL EFFECTS OF A CERTAIN TREATMENT IN ONE MODEL CANNOT NECESSARILY BE EXTRAPOLATED TO ANOTHER" Accordingly, it is highly unpredictable, whether administering total cellular RNA of spleen cells or mRNA encoding the antigen by intravenous injection would have any effect on the course of an autoimmune disease or an allergy, particularly, considering that most of the allergy and autoimmune diseases have distinct etiologies and phenotypes. Accordingly, it is not appropriate to use the results from an allogenic graft response as the support for inducing tolerance to autoimmune disease and allergy.

Claim 43 recites, "administering antigen RNA to the subject", however the specification fails to teach how to obtain the many antigens which are unknown for

autoimmune diseases and allergies. In view of such, the specification fails to support what is claimed.

The Declaration further states (point 8) that example 4 of the specification administering tumor cell total RNA could also be considered as transplanted tissue. While true, the cells used for RNA preparation are allogenic, and the administered in multiple does that last about 21 days, and the last dose being seven days prior to the tumor challenge (transplantation).

The Declaration further asserts (point 9) that the tolerance results observed with tumor cells and skin grafts support similar tolerization to autoantigens and allergens without addressing the differences among the tumor immunity, transplantation immunity, allergic hypersensitivity, and autoimmunity which were discussed in the previous Office actions (Paper #5, page 5; #8, page 4; #17, pages 6-8; and #20, pages 3-4), thus, fails to provide sufficient support for the full scope of the claims. Concerning this aspect, the Remark submitted 12/15/03 alleges that the Examiner does not provide a specific basis for this personal opinion and relying on DNA vaccine references that purportedly demonstrate the distinctiveness of host responses to different types of antigens. In response, the specific basis is provided in the very first Office action (paper #5, page 5), i.e. tolerance induction involves complicated immune regulation. It is well known that the human immune system has a sophisticated mechanism of self and non-self recognition and self-tolerance, a complex negative selection and autoreactive cell-elimination process. Induction of tolerance requires many factors working in concert, such as the type of antigen, the amount of antigen, the timing of antigen priming, and the state of

host immune system etc. These are well-known common knowledge in the art, thus, served as an Official Notice, which is permissive where the facts asserted to be well-known in the art, are capable of instant and unquestionable demonstration as being well-known, and are made in the first Office action (37 CFR 1.113 a, b). This basis has been further expanded in the subsequent office actions. To adequately traverse such a finding, an applicant must specifically point out the supposed errors in the examiner's action, which would include stating the noticed fact is not considered to be common knowledge (37 CFR 1.113 c). "IN THE ABSENCE OF ANY DEMAND BY APPELLANT FOR THE EXAMINER TO PRODUCE AUTHORITY FOR HIS STATEMENT, WE WILL NOT CONSIDER THIS CONTENTION" (*Chevenard*, 139 F.2d at 713, 60 USPQ at 241). In the subsequent responses to Office actions in this case, applicants have not dispute the fact. Even now, applicants fail to state that the basis of the Office rejection is not a well-known common knowledge. Nevertheless, in response to applicant's remark, enclosed are some of the teachings in the art that are evidence for the Official Notice. *Janeway et al* (Chapter 13, Immunobiology 2001, enclosed). *Malone et al* (US 6,110,898) teach delivering a recombinant immunogen and association with tolerance induction. "MUCOSAL ANTIGEN PRESENTATION CAN BE ASSOCIATED WITH EITHER IMMUNOLOGIC STIMULATION OR INDUCTION OF TOLERANCE", "LIKE THE SYSTEMIC IMMUNE COMPARTMENT, THE COMMON MUCOSAL IMMUNE SYSTEM REQUIRES MECHANISMS FOR SELECTIVE SWITCHING BETWEEN THE EXPANSION OF EFFECTOR CELLS AND THE INDUCTION OF TOLERANCE", "THE MECHANISM(S) INVOLVED IN SWITCHING BETWEEN INDUCTION OR SUPPRESSION OF MUCOSAL IMMUNE RESPONSES REMAIN TO BE RESOLVED"(Column 2).

The DNA references cited to illustrate that a host subject would respond differently to different antigens, whether it is encoded by a DNA or RNA, the issue more relevant to the distinctiveness of RNA vaccines lies on the means of delivery, i.e. how to reach the target cells without degradation. As taught by *Qui et al* (gene therapy 1996;3:262-8, IDS AT35) "RNA-MEDIATED GENE TRANSFER IS CLINICALLY MORE DESIRABLE THAN A DNA-MEDIATED METHOD", "SUCCESS IN UTILIZING IN VIVO RNA DELIVERY FOR TRANSGENE EXPRESSION HAS BEEN EXTREMELY LIMITED, PARTIALLY DUE TO RNA INSTATBILITY AND TO THE LACK OF AN EFFICIENT INTRACELLULAR DELIVERY MECHANISM APPLICABLE TO A WIDE VARIETY OF TISSUE OR ORGAN SYSTEMS". Accordingly, it is appropriate to reference a DNA publication for showing the divergent response to different nucleic acid antigens. And it is also appropriate to require the support of the specification commensurate with the scope of the claims. 35 U.S.C. § 112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In re Fisher, 166 USPQ 18, 24 (CCPA 1970).

Accordingly, for reasons of record and those set forth above, the disclosure fails to meet the statutory enablement requirement.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Qiu et al* (Gene Ther 1996;3:262-68, IDS), taken with *Nair et al* (US 5,853,719, IDS).

The claims are directed to a method of inducing an immune response to a tumor comprising administering total tumor RNA to epidermal cells *in vivo*.

Qiu et al teach gene gun delivery to epidermal cells in vivo mRNA encoding a model antigen (hAAT), and immune responses induced to the specific antigen in mice (e.g. abstract). *Qui et al* go on to teach this approach could be used to develop vaccines for cancer immunotherapy (left column, page 267). *Qui et al* do not teach using the total tumor RNA. However, before the effective filing date of the instant application, *Nair et al* (US 5853719) teach "FOR CONVENIENCE, AN RNA-ENRICHED TUMOR PREPARATION CAN BE USED IN LIEU OF PURIFIED RNA. THE INVENTION THUS CIRCUMVENTS THE NEED PURIFY RNA OR ISOLATE AND IDENTIFY A TUMOR ANTIGEN." "EVEN UNFRACTIONATED RNA PREPARATION (E.G. TOTAL RNA OR POLYA+RNA) CAN BE USED, IT IS NOT NECESSARY THAT A TUMOR OR PATHOGEN ANTIGEN BE IDENTIFIED."

Accordingly, it would have been obvious to one of ordinary skill in the art, at the time the effective filing date, to substitute the model antigen mRNA taught by *Qiu et al*, with the total tumor cellular RNA as taught by *Nair et al* with a reasonable expectation of success. One of ordinary skill in the art would have been sufficiently motivated to do so for convenience, i.e. avoiding the trouble of purification step, or of identification of tumor pathogen, with a reasonable expectation of success. Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Qiu et al* (Gene Ther 1996;3:262-68, IDS), and *Nair et al* (US 5,853,719, IDS) as applied to claim 32 above, and further in view of *Segal et al* (US 6,403,080).

The combined teachings of *Qui et al* and *Nair et al* suggest using total tumor cell RNA for inducing an immune response in a subject. *Segal et al* teach that both B16 melanoma and fibrosarcoma cells could be used for developing tumor vaccine (column 29, example 2).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Qui et al* and *Nair et al,* by selecting and employing an antigen of interest such as fibrosacoma as taught by *Segal et al* in the process of vaccine development with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because it is known that fibrosarcoma cells is the subject of tumor vaccine study. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

The prior rejection of claims 2, 3, 5, 7, and 31 under 35 U.S.C. 103(a) as being unpatentable over *Ashley et al* (J Exp Med 1997 Oct;186:1177-82), in view of *Beissert et al* (J Immunol 1995;154:1280-86) now applies to claims 37, 38, 40, 41, and 42.

Applicants argue that there is no motivation for substituting the bone marrow derived dendritic cells of Ashley with the Langerhans cells of Beissert, and the Examiner

fails to provide such teaching, suggestion, and were the reference to be combined, neither references provide reasonable expectation of success.

In response, the Office actions have repeatedly stated, *Beissert et al* teach that epidermal cells particularly the epidermal Langerhens cells are effective antigen presenting cells and have been shown to induce lymphocyte-mediated immune response in a variety of experimental systems both in vitro and in vivo, and that they are particularly indicated in tumor immunity (1st paragraph, page 1280). *Beissert et al* also provided methods of preparing such cells. Accordingly, given the multiple cell types known in the art that could serve as effective antigen-presenting cells, it is within the levels of the skilled in the art to select a type of antigen-presenting cells known in the art for vaccine development with a reasonable expectation of success. Since both *Ashley* and *Beisssert* have shown that the type of antigen-presenting cells could induce an anti-tumor response, the expectation of success is highly reasonable. Applicants are reminded that obviousness does not require absolute predictability of success; for obviousness under 35 U.S.C. § 103, all that is required is a reasonable expectation of success. See In re O'Farrell, 7 USPQ2d 1673 (CAFC 1988). Accordingly, the rejection stands.

It is noted that claim 42 is now included in this rejection because *Ashley et al* use GM-CSF-secreting tumor cells for vaccination, which provide evidence that it is well known in the art to apply cytokines for enhancing anti-tumor response. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Ashley et al* and *Beissert et al* by delivering a

cytokine with that of total tumor RNA with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because it is known that the cytokine would enhance an immune response. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

The prior rejection of claims 2, 3, 5, 7, and 31 under 35 U.S.C. 103(a) as being unpatentable over *Nair et al* (US 5,853,719, IDS) or (US 6,306,388), in view of *Beissert et al* (J Immunol 1995;154:1280-86) now applies to claims 37, 38, 40, and 41.

Applicants presented similar arguments as addressed foregoing in the immediate preceding rejection, and for the same reasons as set forth above, the rejection stands.

Claim 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Nair et al* (US 5,853,719, IDS) and *Beissert et al* (J Immunol 1995;154:1280-86) as applied to claims 37, 38, 40, and 41 above, and further in view of *Segal et al* (US 6,403,080) for reasons of record.

Applicants argue that *Segal et al* do not supply the teachings missing in the primary references. In response, it is the combined teachings that made the invention as a whole obvious. Thus, the rejection stands.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Amy Nelson** can be reached on 571-272-0804. The fax numbers for the organization where this application or proceeding is assigned are **703-872-9306**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is **703-308-0196**.

JANICE LI
PATENT EXAMINER

Q. Janice Li
Patent Examiner
Art Unit 1632

QJL
March 7, 2004